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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/290,798	04/13/1999	INGEGERG HELLSTROM	9632-033	1277

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	24

DATE MAILED: 02/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/290,798	HELLSTROM ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-65,71,86 and 93-118* is/are pending in the application.

4a) Of the above claim(s) *59-65,71,86 and 93-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *101-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II in Paper No. 24 is acknowledged. The traversal is on the ground(s) that the immunoconjugate of group I is the same as that of group II. This is not found persuasive because the invention of group I is drawn to an immunoconjugate that has separate and distinct functions from that of group II. The immunoconjugate of group I is drawn to a compound that is able to bind to Lewis Y antigen and is able to internalize into the cell. However, the invention of group II is drawn to an immunoconjugate that binds to and interferes with antibody BR96 binding. These inventions are considered distinct because the functional properties are different. The invention of group I has internalization characteristics while the invention of group II has blocking characteristics. Because the claims of group II recite only competitive inhibition of BR96 and not binding to the same epitope of BR96, it reads on a different and distinct antibody that blocks BR96 interaction with antigen through steric hinderance.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 59-65, 71, 86, and 93-100 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 24. Applicant is reminded to cancel all claims drawn to a non-elected invention.

3. Claims 59-65, 71, 86, and 93-118 are pending in the instant application, claims 59-65, 71, 86, and 93-100 are withdrawn from consideration as being drawn to a non-elected invention. All pending rejections to claims 59-65, 71,86, and 93-100 are herby rendered moot in light of the withdrawal of claims drawn to a non-elected invention.

4. Claims 101-118 are therefore examined on the record.

Information Disclosure Statement

5. The Information Disclosure Statement filed 5/6/2002 (paper no. 21) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112,2nd paragraph

6. Claims 101-118 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claims 101-118 in the recitation of the term "antibody", it is not clear from the specification what the intended antibody is, as such the metes and bounds of the term cannot be determined because of the lack of disclosure in the specification.

8. Regarding claims 101-118 in the recitation of the term "agent" it is not clear from the specification what the intended agent is to encompass, as such the metes and bounds of the term cannot be determined. Does the applicant intended to encompass Diptheria toxin?

Claim Rejections - 35 USC § 112,1st paragraph

9. Claims 101-118 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or immunoconjugate that comprises

antigen binding regions of the CHIBR96 antibody, does not reasonably provide enablement for an immunoconjugate that competitively inhibits the binding of BR96 antibody to the Lewis Y antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or

absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to an immunoconjugate comprising an antibody joined to a therapeutic agent, wherein the said antibody is capable of competitively inhibiting the binding of BR96 (a monoclonal antibody with ATCC accession number HB-10036).

The amount of direction or guidance present and the presence or absence of working examples: The instant specification teaches that the antibody termed BR96 is capable of binding to carcinoma cells of breast, lung, colon, and ovary origin, and that the BR96 antibody is able to internalize within these cell types. The specification also teaches that the BR96 antibody is toxic to cells independent to any other agents or compounds and is able to elicit antibody dependent cellular cytotoxicity (ADCC) and complement dependent cellular cytotoxicity (CDCC). The specification then teaches that a chimeric antibody termed ChiBR96 (ATCC Accession number HB-10460) is also able to mediate the same effects as that of BR96. However, the specification has not taught any other antibody or immunoconjugate that is capable of competitively inhibiting BR96 antibody. Because the scope of the claims are broad and encompass any antibody or immunoconjugate that competitively inhibits the binding of BR96, it reads on any antibody or immunoconjugate that is capable of binding to or in the general vicinity of the epitope recognized by BR96 thereby competitively inhibiting the binding of BR96. This type of competitive inhibition would be mediated primarily through directly binding to the same epitope of BR96 or steric hinderance. Because the specification has only

taught one such antibody, namely ChiBR96, and no other, and because the claims read on any and all antibodies that are capable of binding to and competitively inhibiting the binding of BR96, one of skill in the art would be forced into undue experimentation to find all potential antibodies/immunoconjugates that fall within the scope of the claims.

Therefore, the specification has only enabled the speciimmunoconjugates comprising antigen binding regions of ChiBR96 joined to a therapeutic compound. The specification has *not* enabled the genus of immunoconjugates that are capable of competitively BR96 antibody.

The breadth of the claims and the quantity of experimentation needed: Given the broad range of immunoconjugates encompassed by the claims, and lack of teachings to correspond to the broad range of immunoconjugates encompassed by the claims, it would require undue experimentation by one of skill in the art to be able to make and practice the invention commensurate in scope with the claims.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 101-109, and 112-118 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-29, and 32-33 of U.S. Patent No. 5980896. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of U.S. Patent No. 5980896 are drawn to an immunoconjugate that comprises ChiBR96 fused to an cytotoxin , specifically Pseudomonas exotoxin A wherein the cell binding domain of the toxin has been removed. The claims of the instant invention is drawn to a broad range of immunoconjugates that fall within the same scope of the U.S. Patent 5980896. The species claimed in U.S. Patent 5980896 thereby obviates the genus claimed in the instant invention.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 101, 102, 104, 105,107,108, 117, and 118 are rejected under 35 U.S.C. 102(b) as being anticipated by Zara *et al* (Anal Biochem 1991 Apr;194(1):156-62). Currently, claims are interpreted as a immunoconjugate that is able to competitively inhibit the binding of BR96 to a carcinoma cell. Zara *et al* teach a derivatized human bifunctional monoclonal antibody directed against a carcinoma cell. Because the bifunctional antibody disclosed by Zara *et al* is cross-linked to other agents, it is thereby considered a chimeric molecule.

Claim Rejections - 35 USC § 102

14. Claims 101-103, 108-109, and 116-118 are rejected under 35 U.S.C. 102(b) as being anticipated by Yeh *et al* (Int. J. Cancer 1992 May;51(2):274-82). Currently, claims are interpreted as a immunoconjugate that is able to competitively inhibit the binding of BR96 to a carcinoma cell. Yeh *et al* teach a immunoconjugate comprising a monoclonal antibody portion and a cytotoxic portion, that recognizes an antigen on the surface of a carcinoma cell, wherein the monoclonal antibody portion is made up of a F(ab')2 and the cytotoxic portion is Doxorubicin. Yeh *et al* further disclose that the administration of the immunoconjugate was effective in treatment of cervical carcinoma.

Claim Rejections - 35 USC § 103

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. Claims 101-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abe *et al* (1986) in view of Oldham *et al* (1986)-note: both references have been cited in previous office actions. Claims are drawn to an immunoconjugate that comprises an antibody, that is capable of competitively inhibiting the binding of BR96, and a therapeutic agent.

Abe *et al* teach an antibody termed AH6 that is able to react with Lewis Y antigen on a colon carcinoma cell. Abe *et al* however, do not specifically teach the conjugation of the AH6 antibody to any therapeutic agent. Oldham *et al,* however do teach that antibodies can be coupled to therapeutic agents and that such conjugations or immunoconjugates are useful in the treatment of cancer.

Therefore, it would have been *prima facie* obvious to one of skill in the art at the time of the invention to make an immunoconjugate comprising an antibody, that was able to competitively inhibit the binding of BR96, and a therapeutic agent because Abe *et al* taught an antibody that was, in the absence of evidence to the contrary, able to bind to and inhibit the binding of BR96 to Lewis Y antigen, and Oldham *et al* suggested that conjugation of therapeutic agents to antibodies would be an effective means of treating cancer. One of ordinary skill in the art would have been motivated to make and practice the instant invention because it is well known in the art that antibodies directed to surface antigens are potential targets for treatment of diseases and that coupling an agent to an antibody was an effective means to deliver said agent to a specific site. Because the antibody taught by Abe *et al* was able to bind to Lewis Y antigen, it would be a good antibody to use block BR96 antibody binding to Lewis Y antigen. And because it was already established in the art that immunoconjugates are a effective in directing agents to a specific site, one of ordinary skill in the art had all the essential elements to make the instant invention. The artisan would have expected a reasonable amount of success in making the instant immunoconjugate because the manipulation of antibodies (i.e. humanization, chimerization, and or fusion) was already well established in the art and the combination of different antibody fragments with different therapeutic agents would have been accomplished easily through routine experimentation.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
January 27, 2003

ALI R. SALIMI
PRIMARY EXAMINER